Remarks

Claims 1-9 are pending in the application. Claims 1, 5, 6, 8 and 9 have been amended.

I. Summary of the Amendment

The specification has been amended to insert a reference to the priority application as instructed by the Examiner, and to change the phrase "(D)-4-aminobutyric acid" to the phrase "4-aminobutyric acid." Support for this latter amendment is at page 6, line 24-25 of the application as filed.

Claim 1 has been amended to (a) clarify the expression "or fragment thereof", and (b) to indicate that the chelating moiety is a peptide chelating moiety capable of complexing a radionuclide in an N_4 configuration.

Claim 5 has been amended to clarify the chemical structure, to correct the symbol "Aba*," and to place a period at the end of the claim.

Claim 6 has been amended to remove an element that is already recited in claim 1.

Claim 8 has been amended to correct the dependency.

Claim 9 has been amended to depend from claim 1 as suggested by the Examiner.

Support for the amendment regarding the radiolabeling moiety in claim 1 is found in Applicant's specification at page 6, line 19-21. Support for the remaining claim amendments is found in the claims as originally filed.

II. Response to Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 1-9 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly ambiguous for reciting the phrase "or fragments thereof." According to the Examiner, this phrase could encompass single amino acids

Claim 1 has been amended herein to clarify that the phrase "or fragments thereof" refers to peptide fragments. A peptide is defined (Bennett, Concise Chemical and Technical Dictionary, Chemical Publishing Company, 1974, page 792; enclosed) as a "derived protein substance containing two or more amino acids joined together by a peptide linkage." Based upon this definition, one of ordinary skill in the art would understand the meaning of the phrase "or peptide fragments thereof" in claim 1 to refer to a peptide fragment that is a two amino acid segment of the tri-peptide of SEQ ID NO. 1.

Claim 5 has been rejected as indefinite because the structure as drawn is alleged to be difficult to read and because the symbol "Aba*" is allegedly unclear. Applicant has redrawn the chemical structure to eliminate the crowding of the bonds about the Tc atom. The symbol "Aba*" is an error which has been corrected in claim 5 and in Fig. 1 to remove the asterisk (*). The correct symbol, "Aba" is defined in Applicant's specification in the paragraph beginning at page 6, line 19 as "4-aminobutyric acid." The definition of "Aba" was amended by a preliminary amendment filed June 4, 2001 to erroneously read "(D)-4-aminobutyric acid." The definition of "Aba" is amended herein to again read "4-aminobutyric acid," as in the application as filed.

No new matter has been added by these amendments. The claims as amended herein are clear, definite, and in compliance with the second paragraph of 35 U.S.C. §112. Applicant therefore respectfully requests that the rejection of claims 1-9 under 35 U.S.C. §112, second paragraph be withdrawn.

III. Response to Rejection under 35 U.S.C. § 102(e)

Claims 1-4 and 7-9 are rejected under 35 U.S.C. 102(e) as allegedly anticipated by Dean *et al.* Applicant respectfully disagrees.

For a reference to anticipate a claim, every limitation of that claim must identically appear, either expressly or inherently, in the reference. In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). Absence of any claim element from the reference "negates anticipation." *Kloster Speedsteel AB v. Crucible, Inc.*, 230 USPQ 81, 84 (Fed. Cir. 1986); *Rowe v. Dror,* 42 USPQ2d 1550, 1552 (Fed. Cir. 1992).

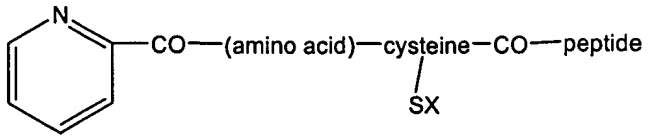
The Examiner has alleged that "both Applicant and Dean *et al.* disclose compositions comprising the peptide Gly-Pro-Arg having a radiolabel binding moiety." Claim 1 of the present invention, as amended herein, recites a structure including a group, M, which is a radiolabeling moiety "comprising a peptide chelating moiety capable of complexing to a selected radionuclide in an N_4 configuration." Dean *et al.* does not teach a peptide having a radiolabeling moiety corresponding to Applicant's group M, as now defined in claim 1.

Dean *et al.* teach peptides that are radiolabeled. However, the peptides disclosed by Dean *et al.* are radiolabeled by being covalently bound to a Tc-99m binding moiety that is specifically defined as having one of the following six structures:

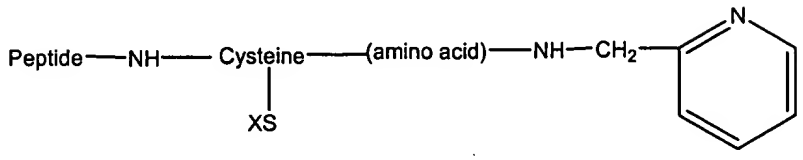
1. $C(pgp)_s$—(aa)—$C(pgp)_s$, wherein aa is any amino acid and $C(pgp)_s$ is a protected cysteine.

2. A- CZ(B)-[C(RR')]$_n$-X, wherein one of X or B is -SH

3.



4.



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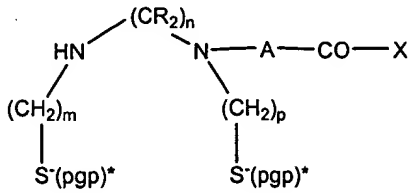
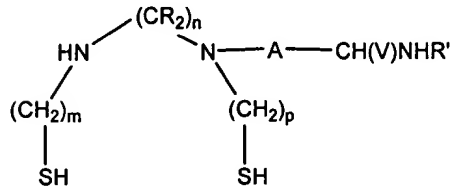


6.



The claims, as herein amended, recite peptides that contain a radiolabeling moiety M that is a peptide chelating moiety capable of binding with a selected radionuclide in an N_4 configuration. Dean *et al.* does not disclose any peptide containing a peptide radionuclide binding moiety capable of binding a radionuclide in an N_4 configuration. None of the six Tc-99m binding moieties reproduced above, represents a peptide chelating moiety capable of binding a radionuclide in an N_4 configuration. Structure 1 is a three-amino acid moiety comprising two protected cysteines. Structure 1 could not chelate a radionuclide in an N_4 configuration. Structure 2 is a functionalized 1, 2 or 3 carbon chain which is not a peptide structure. Moreover, structure 2 cannot chelate a radionuclide in an N_4 configuration. Structures 3 and 4 are picolyl derivatives of two-amino acid moieties which cannot chelate a radionuclide in an N_4 configuration. Structures 5 and 6 are bis-amino-bis-thiol moieties and cannot chelate a radionuclide in an N_4 configuration.

Dean *et al.* thus does not anticipate the compositions of the present invention because Dean does not disclose a compound comprising the chelating moiety recited in claim 1 as herein amended. Applicant respectfully requests withdrawal of the rejection of claims 1-4 and 7-8 under 35 U.S.C. §102.

IV. Response to Rejection under 35 U.S.C. § 103(a)

Claims 1-4, 7 and 8 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dean *et al.*, in view of Kawasaki *et al.* and Laudano *et al.*

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (MPEP 706.02(j))

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

MPEP 706.02 states that "[A]fter indicating that the rejection is under 35 U.S.C. 103, there should be set forth (1) the difference or differences in the claim over the applied reference(s), (2) the proposed modification of the applied reference(s) necessary to arrive at the claimed subject matter, and (3) an explanation why such proposed modification would be obvious." Applicant respectfully submits that the Examiner has not established that the claimed invention is *prima facie* obvious over Dean *et al.*, in view of Kawasaki *et al.* and Laudano *et al.*, each of which contains at least one thiol moiety that generates a binding interaction when coordinating technetium.

As stated above, Dean *et al.* teach peptides that are radiolabeled by covalent binding to a Tc-99m binding moiety that is one of a group of six defined, sulfur-containing structures.

Kawasaki *et al.* disclose various peptides that are analogs of the N-terminal portion of fibrin α-chain and which are examined for effects on fibrinogen/thrombin clotting.

Laudano *et al.* disclose peptides corresponding to the amino termini of fibrin α- and β-chains, fibrinogen binding affinity of the disclosed peptides, and fibrin polymerization inhibition activity of the disclosed peptides.

The Examiner alleges that it would be obvious to modify Dean *et al.* to generate various analogs and fragments of Gly-Pro-Arg that bind fibrin, and to conjugate such peptides to a radiolabeling moiety.

However, the combination of the cited references does not teach or suggest all the elements of the claimed invention. Dean *et al.* fails to teach the element of a peptide that is bound to a peptide radiolabeling moiety capable of complexing with a radionuclide in an N_4 configuration.

Combination of the teaching of Dean *et al.* with teachings of Kawasaki *et al.* and/or Laudano *et al.* does not add any teaching or suggestion of the claimed radiolabeling moiety. Even were Dean *et al.* to suggest combining the Dean *et al.* radiolabeling moiety to the peptides taught by Kawasaki and/or Laudano (which suggestion is not made), the numerous radiolabeling moieties taught by Dean (reproduced above) are structurally and functionally distinct from the peptide chelating moiety of the invention which is recited as capable of complexing with a radionuclide in an N_4 configuration. As mentioned above, all of the radiolabeling moieties taught by Dean comprise at least one sulfur having a binding interaction in coordinating to technetium. Thus, the chelating moieties of Dean *et al.* cannot complex a radionuclide in an N_4 configuration. Moreover, there is no teaching or suggestion in Dean *et al.* that N_4 amino acid chelators can or should be substituted for the sulfur-containing chelators of Dean *et al.*

Dean *et al.*, alone or in combination with the other cited references, neither teaches nor suggests the element of a peptide radiolabeling moiety that complexes a radionuclide in an N_4 configuration as recited in the present claims. Applicant therefore respectfully requests that the Examiner withdraw the rejection of claims 1-4 and 7-8 under 35 U.S.C. §103(a).

Conclusion

Applicant believes this response and claim amendment to be fully responsive to the Examiner's Office action. Applicant submits that the claims as herein amended are novel and nonobvious over the cited art and are not indefinite. Applicant therefore respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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